

**REMARKS**

In the Office Action dated September 8, 2003, claims 1-10, 16-19, 26, 30, and 31, all of the claims under consideration of the subject patent application, were rejected. By amendment above, claims 1-10, 16-19, 26, 30, and 31 have been cancelled without prejudice, and new claims 39-53 have been added to the application. Support for new claims 39-53 can be found on page 7 line 21-page 8, line 6 , and previously presented claims 1-10, 16-19, 26, 30 and 31. Additionally, new claim 53 is also directed to the previously unexamined range of the carrier material being present in an amount of 45-55% by weight, support for which can be found on page 9 lines 24-29.

Reconsideration of this application and allowance of the claims is respectfully requested in view of the foregoing amendments and the following remarks.

Claims 1-10, 16-19, 26, 30, and 31 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Geyer et al. (5,380,535) and Elger et al. (4,844,907). According to the Examiner the recitations "adapted to disintegrate quickly in the gastro-intestinal tract" in claims 1 and 16 and "is obtained by compressing said ...." in claims 1 and 16 do not render the claimed compositions nonobvious over the prior art because the recitation "adapted to disintegrate quickly in the gastro-intestinal tract" is considered to be intended use of the composition herein and/or an inherent property which will not further limit claims drawn to a composition or product. The Examiner further asserted that the determination for a product-by-process claim is based on the product itself. Thus according to the Examiner the patentability of the product does not depend on its method of production and the claims to a product in the product-by-process claim is unpatentable if the product is the same or obvious from a product of the prior art. The

Examiner asserted therefore, that the recitation “is obtained by compressing said ....” in claims 1 and 16 is not considered a limitation of the composition herein. According to the Examiner Geyer et al. clearly teaches that the composition therein comprises sodium bicarbonate in 0.1 to about 20 % weight, and the formulations of ibuprofen in 0.1-75% or 0.5-40% weight in compressed tablet form comprising the instant ingredients are also clearly taught. Therefore, according to the Examiner there is motivation to combine Geyer et al. and Elger et al. to make the present invention.

Applicant submits that the invention of the present application provides an improved compressed dosage form which permits delivery of high therapeutic levels of the sodium salt of racemic ibuprofen to the gastrointestinal tract of a patient. The sodium salt of racemic ibuprofen is a flaky, soft and sticky material. Consequently, it does not lend itself to formulation into a directly compressed dosage form as it typically sticks to the tableting punches. Moreover, it is also difficult to pre-granulate the sodium salt prior to compression with other excipients. Therefore, in order to form satisfactory compressed dosage forms of the sodium salt of racemic ibuprofen it is necessary to pre-treat the salt such as by milling, etc.

Unexpectedly, the inclusion of sodium bicarbonate or sodium carbonate in the carrier material permits the formation of a satisfactory compressed dosage form of the sodium salt of racemic ibuprofen without the need to initially pre-treat the ibuprofen. Conveniently, it is therefore possible to use sodium ibuprofen taken directly from a bulk production process, thereby significantly reducing the overall production costs.

In addition, the inclusion of sodium bicarbonate or sodium carbonate also enhances the compressibility of the pharmaceutical composition comprising the compressible filler and

disintegrant. Thus, the composition used to form the compressed dosage form may be compressed by applying compression forces of standard tableting machines to produce a compressed dosage form which exhibits improved hardness (i.e. so that it does not break up during further manufacturing steps) while maintaining an acceptable relatively fast disintegration time to permit an onset hastened action as discussed on page 2, lines 1 to 20, and page 3, lines 8 to 14 of the disclosure. This effect is clearly demonstrated by the results of Tables 1 and 2 and the commentary thereon at page 31. Furthermore, the inclusion of sodium bicarbonate or sodium carbonate permits a reduction in the overall amount of compressible filler thereby allowing production of an acceptably sized tablet including a large therapeutic dose of the sodium salt of racemic ibuprofen as is described on page 2, lines 4 to 8 and page 3, lines 7 to 10 of the disclosure.

In contrast to the present invention, Geyer et al. (U.S. 5,380,555) solves a completely different technical problem than the one solved by the invention of the present application. Geyer et al. is concerned with providing a chewable pharmaceutical composition which is designed to be chewed and swallowed while masking the taste of the unpalatable drug as described in column 1, lines 14 to 20, column 1, lines 61 to 65, and column 2, lines 8 to 14 of Geyer et al. In other words, Geyer et al. is concerned with taste masking unpalatable drugs, and it is not concerned whatsoever with providing an improved process which permits formation of an improved compressed dosage form of the sodium salt of racemic ibuprofen as claimed in the present invention. Geyer et al. does not teach or suggest that the inclusion of sodium bicarbonate or sodium carbonate in combination with the sodium salt of racemic ibuprofen would permit the ibuprofen to be compressed directly on standard tableting machines without the need to pretreat

the ibuprofen to form a dosage form with improved hardness and an acceptable disintegration time.

In this respect, the sodium bicarbonate additive which may be used in the composition of Geyer et al. is employed as a “buffering agent” to eliminate the unpleasant taste of the drug as described in column 6, lines 16 to 24 of Geyer et al. In this respect it is well known that sodium bicarbonate is basic, whereas ibuprofen free acid is acidic. Thus, as stated in Geyer et al. the sodium bicarbonate is added to acidic ibuprofen free acid to regulate or “buffer” the pH of the free acid, thereby improving the palatability of the ibuprofen. Geyer et al. does not teach or suggest that the sodium bicarbonate would permit the sodium salt of racemic ibuprofen to be compressed directly without the need for pre-treating the ibuprofen. Geyer et al. simply do not suggest employing the sodium salt of racemic ibuprofen.

Contrary to the Examiner’s opinion, a skilled person on reading Elger et al. (US 4,844,907) would not be motivated to replace the ibuprofen free acid of Geyer et al. with the sodium salt of racemic ibuprofen in the expectation of providing the advantages of the present invention as discussed above.

Elger et al. solves a different technical problem than Geyer et al., and as such these documents are technically incompatible. Elger et al. is concerned with providing a multi-layered tablet comprising a narcotic and an anti-inflammatory drug which exhibits a desired crushing strength and acceptable disintegration time as described in column 1, lines 39 to 40, and in the comparative Examples A to D and Examples 1 to 8 of Elger et al., whereas Geyer et al. relates to providing a chewable composition while masking the taste of an unpalatable drug. Moreover, Geyer et al. does not mention employing the sodium salt of racemic ibuprofen in the compressed

dosage form and neither does Elger et al. In fact Elger et al. does not even mention sodium ibuprofen. Furthermore, applicant notes that neither Geyer et al. nor Elger et al. mention the use of sodium carbonate.

In addition, Geyer et al. explicitly teaches away from employing the sodium salt of racemic ibuprofen. Geyer et al. teaches the skilled person that a preferred method of taste masking an unpalatable drug comprises forming a melt at mildly elevated temperatures of 55°C which comprises a molten lipid phase and preferably a molten phase of both the lipid and drug (column 3, lines 25 to 30 and lines 34 to 41). In particular, Geyer et al. teaches that the drugs which are most advantageously employed are those such as ibuprofen which are solid at room temperature but which have good thermal stability and low melting points, i.e., they may be readily liquefied by heat.....generally at temperatures no greater than about 95°C (column 4, lines 3-11). In this respect, ibuprofen free acid has a melting point of approximately 75 to 78°C whereas the sodium salt of racemic ibuprofen has a melting point of around 200°C.

Therefore, applicant submits that the use of sodium bicarbonate or sodium carbonate in a compressed dosage form of the sodium salt of racemic ibuprofen is not obvious over the combination of Geyer et al. and Elger et al.

Applicant respectfully submits that the claimed invention in claims 1-10, 16-19, 26, 30 and 31 therefore is not obvious over US 5,380,535 (Geyer et al) in combination with US 4,844,907 (Elgar et al.). Withdrawal of the rejection is respectfully requested and applicant submits that claims 39-53 are therefore also patentable.

Claims 1-10, 30 and 31 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Geyer et al. (US 5,380,535) and Gregory et al. (US 5,262,179). According to

the Examiner adding the recitations “adapted to disintegrate quickly in the gastro-intestinal tract” in claims 1 and 16 and “is obtained by compressing said ....” in claims 1 and 16 do not render the claimed compositions nonobvious over the prior art. The Examiner made the same assertions when rejecting these claims over Geyer et al and Elger et al as is discussed above. According to the Examiner Greyer et al clearly teaches that the composition therein comprises sodium bicarbonate in 0.1 to about 20 % weight, and the formulations of ibuprofen in 0.1-75% or 0.5-40% weight in compressed tablet form comprising the instant ingredients are also clearly taught. Therefore, according to the Examiner there is motivation to combine Geyer et al. and Gregory et al. to make the present invention.

Similarly as discussed above applicant submits that the present application is directed to a solid non-effervescent compressed dosage form comprising a racemic ibuprofen medicament in the form of a sodium salt and sodium bicarbonate or sodium carbonate. For the reasons discussed above Geyer et al. does not teach or suggest the compressed dosage form as claimed in the present invention.

Contrary to the Examiner’s opinion, applicant respectfully submits that a skilled person on reading Gregory et al. (US 5,262,179) would not be motivated to replace the ibuprofen free acid of Geyer et al. with the sodium salt of racemic ibuprofen in the expectation of providing the advantages of the present invention as discussed above.

Gregory et al. solves a different technical problem than Geyer et al., and as such these documents are technically incompatible. Gregory relates to taste masking aqueous solutions of ibuprofen salts as described in column 2, lines 62 to 66 and column 4, lines 3 to 11 of Gregory et al., whereas Geyer et al. relates to providing a chewable composition while masking the taste of

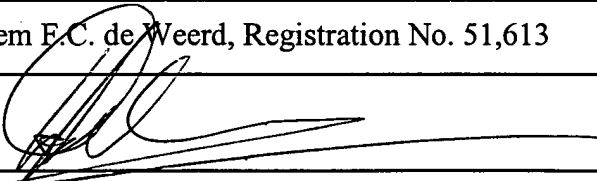
an unpalatable drug. Although Gregory employs sodium ibuprofen this is used because of its increased water solubility and the compositions of Gregory et al. are designed to be administered as an aqueous solution as described in column 2, lines 22 to 25 and column 4, lines 3 to 7 of Gregory et al. Alkali metal bicarbonates employed are used in Gregory as a taste masking agent (column 3, lines 30 to 32), and there is no mention at all that sodium bicarbonate in combination with sodium ibuprofen, a compressible filler and a disintegrate would permit the sodium ibuprofen to be compressed directly without the need for pre-treating the ibuprofen. In this respect, we note all of the specific examples of Gregory which employ sodium bicarbonate are directed to dry powdered formulations. Moreover, Geyer et al. does not mention employing the sodium salt of racemic ibuprofen in the compressed dosage form. Furthermore, applicant notes that neither Geyer et al. nor Gregory et al. mention the use of sodium carbonate.

Furthermore, Geyer et al. explicitly teaches away from employing the sodium salt of racemic ibuprofen. Geyer et al. teaches the skilled person that a preferred method of taste masking an unpalatable drug comprises forming a melt at mildly elevated temperatures of 55 °C which comprises a molten lipid phase and preferably a molten phase of both the lipid and drug (column 3, lines 25 to 30 and lines 34 to 41). In particular, the drugs which are most advantageously employed are those such as ibuprofen which are solid at room temperature but which have good thermal stability and low melting points, i.e., they may be readily liquefied by heat.....generally at temperatures no greater than about 95 °C (column 4, lines 3-11). In this respect, ibuprofen free acid has a melting point of approximately 75 to 78 °C whereas the sodium salt of racemic ibuprofen has a melting point of around 200 °C.

Therefore, applicant submits that the use of sodium bicarbonate or sodium carbonate in a compressed dosage form of the sodium salt of racemic ibuprofen is not obvious over the combination of Geyer et al. and Gregory et al.

Applicant respectfully submits that the claimed invention in claims 1-10, 30 and 31 therefore is not obvious over US 5,380,535 (Geyer et al) in combination with US 5,262,179 (Gregory et al). Withdrawal of the rejection is respectfully requested and applicant respectfully submits that claims 39-53 are therefore also patentable.

Applicant submits that the present application is now in condition for allowance.  
Reconsideration and favorable action are earnestly requested.

RESPECTFULLY SUBMITTED,					
NAME AND REG. NUMBER	Willem F.C. de Weerd, Registration No. 51,613				
SIGNATURE				DATE	Feb. 6, 2004
Address	Rothwell, Figg, Ernst & Manbeck 1425 K Street, N.W., Suite 800				
City	Washington	State	D.C.	Zip Code	20005
Country	U.S.A.	Telephone	202-783-6040	Fax	202-783-6031